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USPT	112 same 18	6	<u>L14</u>
USPT	12 same 18	10	<u>L13</u>
USPT	19 or 110 or 111	39502	<u>L12</u>
USPT	picornavirus or picornaviral or antiviral	9119	<u>L11</u>
USPT	cold near4 (flu or cough)	475	<u>L10</u>
USPT	rhinitis or rhinovirus or rhinoviral or viral or virus	36789	<u>L9</u>
USPT	14 or 15 or 16	2542	<u>L8</u>
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USPT	(phenyl) adj (methyl or ethyl or alkyl) adj ketone	174	<u>L6</u>
USPT	(phenylmethyl or phenylethyl or phenylalkyl) adj ketone	88	<u>L5</u>
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<u>S411</u>	USPT	((rhinitis or rhinovirus or rhinoviral or viral or virus)or (cold near4 (flu or cough))or (picornavirus or picornaviral or antiviral)) same ((phenylketone or phenyl ketone)or ((phenylmethyl or phenylethyl or phenylalkyl) adj ketone)or ((phenyl) adj (methyl or ethyl or alkyl) adj ketone))
<u>S410</u>	USPT	((trifluoromethyl or trifluoro adj methyl))adj3 ketone) same ((phenylketone or phenyl ketone)or ((phenylmethyl or phenylethyl or phenylalkyl) adj ketone)or ((phenyl) adj (methyl or ethyl or alkyl) adj ketone))
<u>S409</u>	USPT	(rhinitis or rhinovirus or rhinoviral or viral or virus) or (cold near4 (flu or cough)) or (picornavirus or picornaviral or antiviral)
<u>S408</u>	USPT	picornavirus or picornaviral or antiviral
<u>S407</u>	USPT	cold near4 (flu or cough)
<u>S406</u>	USPT	rhinitis or rhinovirus or rhinoviral or viral or virus
<u>S405</u>	USPT	(phenylketone or phenyl ketone) or ((phenylmethyl or phenylethyl or phenylalkyl) adj ketone) or ((phenyl) adj (methyl or ethyl or alkyl) adj ketone)
<u>S404</u>	USPT	l4-l6
<u>S403</u>	USPT	(phenyl) adj (methyl or ethyl or alkyl) adj ketone
<u>S402</u>	USPT	(phenylmethyl or phenylethyl or phenylalkyl) adj ketone
<u>S401</u>	USPT	phenylketone or phenyl ketone
<u>S400</u>	USPT	((trifluoromethyl or trifluoro adj methyl))adj3 ketone) near4 6\$phenyl
<u>S399</u>	USPT	((trifluoromethyl or trifluoro adj methyl)) adj3 ketone
<u>S398</u>	USPT	(trifluoromethyl or trifluoro adj methyl)
<u>S397</u>	USPT	(differentiation adj factor adj (1 or I))
<u>S396</u>	USPT	((530/330)[COR])and (hiv or aids)) and (peptide or tetrapeptide)
<u>S395</u>	USPT	peptide or tetrapeptide
<u>S394</u>	USPT	((530/330)[COR]) and (hiv or aids)
<u>S393</u>	USPT	hiv or aids

WEST[Help](#)[Logout](#)[Main Menu](#)[Search Form](#)[Posting Counts](#)[Show S Numbers](#)[Edit S Numbers](#)[Generate Collection](#)**Search Results - Record(s) 1 through 6 of 6 returned.**☐ **1. Document ID: US 5985863 A**

Entry 1 of 6

File: USPT

Nov 16, 1999

DOCUMENT-IDENTIFIER: US 5985863 A

TITLE: Compositions and methods for decreasing IGIF and IFN- γ production by administering an ICE inhibitor**DEPR:**

Further examples of ICE inhibitors which may be used according to the embodiments of this invention are those found in U.S. Pat. Nos. 5,008,245; 5,411,985; 5,416,013; 5,430,128; 5,434,248; 5,462,939; 5,486,623; 5,498,616 and 5,498,695; PCT published applications WO 91/15577; WO 93/05071; WO 93/09135; WO 93/14777; WO 93/16710; WO 94/03480; WO 95/05192; WO 95/26958; WO 95/29672; WO 95/33751 and WO 96/03982; Foreign patent documents EP 519,748; EP 528,487; EP 529,713; EP 533,226; EP 547,699; EP 618,223; EP 623,592; EP 623,606; EP 628,550; EP 644,197; EP 644,198; AU 64514/94; DE 195 34 164; and GB 2,292,149; and other documents, such as M. Ator, "Peptide and Non-peptide Inhibitors of Interleukin-1 β . Converting Enzyme", Cambridge Healthtech Institute (Inflammatory Cytokine Antagonists Targets, Strategies, and Indication), (1994), see pyridazines, pages 2-4; peptides, pages 5-13; M. Ator and R. Dolle, "Interleukin-1 β . Converting Enzyme: Biology and the Chemistry of Inhibitors", Curr. Pharm. Design, I, pp. 191-210 (1995); K. Chapman, "Synthesis of a Potent, Reversible Inhibitor of Interleukin-1 β . Converting Enzyme", Bioorg. Med. Chem. Lett., 2, pp. 613-618 (1992); R. Dolle et al., "Aspartyl .alpha.-((1-Phenyl-3-(trifluoromethyl)-pyrazol-5-yl)oxy)methyl Ketones as Interleukin-1 β . Converting Enzyme Inhibitors. Significance of the P.sub.1 and P.sub.3 Amido Nitrogens for Enzyme-Peptide Inhibitor Binding", J. Med. Chem., 37, pp. 3863-3865 (1994), see page 364; R. Dolle et al., "Aspartyl .alpha.-((Diphenylphosphinyl)oxy)methyl Ketones as Novel Inhibitors of Interleukin-1 β . Converting Enzyme. Utility of the Diphenylphosphinic Acid Leaving Group for the Inhibition of Cysteine Proteases", J. Med. Chem., 38, pp. 220-222 (1995), see page 221; R. Dolle et al., "P.sub.1 Aspartate-Based Peptide .alpha.-((2,6-Dichlorobenzoyl)oxy)methyl Ketones as Potent Time-Dependent Inhibitors of Interleukin-1 β . Converting Enzyme", J. Med. Chem., 37, pp. 563-564 (1994), see page 563; R. Dolle et al., "First Examples of Peptidomimetic Inhibitors of Interleukin-1 β . Converting Enzyme", J. Med. Chem., 39, pp. 2438-2440 (1996); P. Elford et al., "Reduction of Inflammation and Pyrexia in the Rat by Oral Administration of SDZ 224-015, an Inhibitor of the Interleukin-1 β . Converting Enzyme", Brit. J. Pharm., 115, pp. 601-606 (1995); I. Fauszt et al., "Inhibition of Interleukin-1 β . Converting Enzyme by Peptide Derivatives", Proc. of the 13th Am. Peptide Symp., June 20-25, 1993, Hodges, R. S. and Smith, J. A., Eds., Peptides, pp. 589-591 (1994); T. Graybill et al., "Preparation and evaluation of peptidic aspartyl hemiacetals as reversible inhibitors of interleukin-1 β . converting enzyme (ICE)", Int. J. Peptide Protein Res., 44, pp. 173-182 (1994); T. Graybill et al., "Synthesis and Evaluation of Diacylhydrazines as Inhibitors of the Interleukin-1 β . Converting Enzyme (ICE)", Bioorg. Med. Chem. Lett., 5, pp. 1197-1202 (1995); B. Miller et al., "Inhibition of Mature IL-1 β . Production in Murine Macrophages

and a Murine Model of Inflammation by WIN 67694, an Inhibitor of IL-1.β. Converting Enzyme", J. Immunol., 154, pp. 1331-1338 (1995), see page 1332; A. Mjalli et al., "Phenylalkyl Ketones as Potent Reversible Inhibitors of Interleukin-1.β. Converting Enzyme", Bioorg. Med. Chem. Lett., 3, pp. 2689-2692 (1993); A. Mjalli et al., "Synthesis of a Peptidyl 2,2-Difluoro-4-Phenylbutyl Ketone and its Evaluation as an Inhibitor of Interleukin-1.β. Converting Enzyme", Bioorg. Med. Chem. Lett., 3, pp. 2693-2698 (1993); A. Mjalli et al., "Activated Ketones as Potent Reversible Inhibitors of Interleukin-1.β. Converting Enzyme", Bioorg. Med. Chem. Lett., 4, pp. 1965-1968 (1994), see page 1967; M. Mullican et al., "The Synthesis and Evaluation of Peptidyl Aspartyl Aldehydes as Inhibitors of ICE", Bioorg. Med. Chem. Lett., 4, pp. 2359-2364 (1994), see page 2362; C. Ray et al., "Viral Inhibition of Inflammation: Cowpox Virus Encodes an Inhibitor of the Interleukin-1.β. Converting Enzyme", Cell, 69, pp. 597-604 (1992); R. Robinson and K. Donahue, "Synthesis of a Peptidyl Difluoro Ketone Bearing the Aspartic Acid Side Chain: An Inhibitor of Interleukin-1.β. Converting Enzyme", J. Org. Chem., 57, pp. 7309-7314 (1992), see page 7309; M. Salvatore et al., "L-741,494, A Fungal Metabolite that is an Inhibitor of Interleukin-1.β. Converting Enzyme", J. Nat. Prods., 57, pp. 755-760 (1994); S. Schmidt et al., "Synthesis and Evaluation of aspartyl .α.-Chloro-, .α.-Aryloxy-, and .α.-Arylacyloxymethyl Ketones as Inhibitors of Interleukin-1.β. Converting Enzyme", Am. Chem. Soc. (208th Natl. Mtg.), MEDI 4, Aug. 21-25 (1994); N. Thornberry et al., "Inactivation of Interleukin-1.β. Converting Enzyme by Peptide (Acyloxy)methyl Ketones", Biochemistry, 33, pp. 3934-3940 (1994), see pages 3937-3938; E. Tsukuda et al., "EI-1507 and -2, Novel Interleukin-1.β. Converting Enzyme Inhibitors Produced by Streptomyces sp. E-1507", J. Antibiotics, 49, pp. 333-339 (1996).

Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	KWIC	Image
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2. Document ID: US 5492689 A

Entry 2 of 6

File: USPT

Feb 20, 1996

DOCUMENT-IDENTIFIER: US 5492689 A

TITLE: Combined virustatic antimediator (COVAM) treatment of common colds

DEPR:

While the antiviral agent used in the investigations was inteferon 52, other antiviral agents which are specific for viruses commonly found in colds should yield the same synergistic cold combatting results when used in combination with antiinflammatory compounds. As suitable examples of antiviral agents that could be used in COVAM therapy, Sperber et al., Antimicrob. Agents Chemother., 32:409-419 (1988), which is herein incorporated by reference, provides a listing of representative antiviral agents with activity against rhinovirus which includes the following: Inteferons (rIFN-.α..sub.2b, rIFN-.α..sub.2a, rIFN-.β..sub.serine), Interferon inducers (Poly I:C, N,N-Dioctadecyl -N', N'-bis-(2-hydroxyethyl) -propanediamine (CP-20,961), Capsid binding agents /inhibitors of uncoating (4',6'-Dichloroflavan (BW 683C), 4'-ethoxy-2'-hydroxy-4,6'-dimethoxychalcone (Ro 09-04 10), 5-ethoxy-3-methoxy-2-(p-methoxy-trans-cinnamoyl)phenylphosphate (Ro 09-0415), 1-(5-tetradecyloxy-2-furanyl)ethanone (RMI 15,731), 2-[-(1,5,10,10a-tetrahydro-3H-thiazolo[3,4b]isoquinolin-3-ylindene)amino]-4-thiazole acetic acid (44,081 .P.), Disoxaril, 5-[7-[4-(4,5-dihydro-2-oxazolyl)phenoxy]heptyl]-3-methylisoxazole (WIN 51,711), 3-methoxy-6-[4-(3-methylphenyl)-piperazinyl]pyradazine (R61837), 3,4-dihydro-2-phenyl-2H-pyrano[2,3-b]pyridines, and phenoxypyridinecarbonitriles), 2-(3,4-dichlorophenoxy)-5-nitrobenzonitrile (MDL 860), Benzoimidazoles (Enviroxime, 2-amino-1-(isopropyl sulfonyl)-6-benzimidazole phenyl ketone oxime), 1'-methyl spiro(adamantane-2,3-pyrrolidine)maleate, Isatin thiosemicarbazone, Fusidic acid, Substituted trizaindoles (4-([8-amino-7-chloro-5-methyl-5H-as-triazino(5,6-b)indol-3-yl]amino)-2-methyl-2-butanol (SK&F 40491)), 2,6-diphenyl-3-methyl-2,3-dihydroimidazo[2,1-b]thiazole (RP 19236), 3-α-naphthyl-5-diethylcarbamoyl-1,2,4-oxadiazole (GL R9-338), Oxolinic acid, Isoquinolines (1-(p-chlorophenoxyethyl)-3,4-dihydroisoquinone hydrochloride (UK-2054), 3,4-dihydro-1-isoquinolineacetamide hydrochloride), 1-p-chlorophenyl-3-(m-3-isobutyl-guanidinophenyl)urea hydrochloride (ICI 73,602),

1-p-chlorophenyl-3-(m-3-isobutyl-guanidinophenyl)urea hydrochloride (ICI 73,602), and zinc salts. Substances which prevent attachment of the rhinovirus to the nasal cells, such as anti ICAM-1 antibody [Hayden et al, Antiviral Res., 9:233-247 (1988)] and synthetic ICAM-1 [Greve et al., Cell, 56:839-847 (1989)], and other types of interferon should also be useful in COVAM therapy.

Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	KWIC	Image
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3. Document ID: US 5422097 A

Entry 3 of 6

File: USPT

Jun 6, 1995

DOCUMENT-IDENTIFIER: US 5422097 A

TITLE: Combined antiviral and antimediator treatment of common colds

DEPR:

While the antiviral agent used in the investigations was inteferon .alpha.2, other antiviral agents which are specific for viruses commonly found in colds should yield the same synergistic cold combatting results when used in combination with antiinflammatory compounds. As suitable examples of antiviral agents that could be used in COVAM therapy, Sperber et al., Antimicrob. Agents Chemother., 32:409-419 (1988), which is herein incorporated by reference, provides a listing of representative antiviral agents with activity against rhinovirus which includes the following: Inteferons (rIFN-.alpha..sub.2b, rIFN-.alpha..sub.2a, rIFN-.beta..sub.serine), Interferon inducers (Poly I:C, N,N-Dioctadecyl-N', N'-bis-(2-hydroxyethyl)-propanediamine (CP-20,961), Capsid binding agents/inhibitors of uncoating (4',6-Dichloroflavan (BW 683C), 4'-ethoxy-2'-hydroxy-4,6'-dimethoxychalcone (Ro 09-0410), 5-ethoxy-3-methoxy-2-(p-methoxy-trans-cinnamoyl)phenylphosphate (Ro 09-0415), 1-(5-tetradecyloxy-2-furanyl)ethanone (RMI 15,731), 2-[-(1,5,10,10a-tetrahydro-3H-thiazolo[3,4b]isoquinolin-3-ylindene)amino]-4-thiazole acetic acid (44,081 R.P.), Disoxaril, 5-[7-[4-(4,5 dihydro-2-oxazolyl)phenoxy]heptyl]-3-methylisoxazole (WIN 51,711), 3-methoxy-6-[4-(3-methylphenyl)-piperazinyl]pyridazine (R61837), 3,4-dihydro-2-phenyl-2H-pyrano[2,3-b]pyridines, and phenoxypyridinecarbonitriles), 2-(3,4-dichlorophenoxy)-5-nitrobenzonitrile (MDL 860), Benzoimidazoles (Enviroxime, 2-amino-1-(isopropyl sulfonyl)-6-benzimidazole phenyl ketone oxime), 1'-methyl spiro(adamantane-2,3-pyrrolidine)maleate, Isatin thiosemicarbazone, Fusidic acid, Substituted trizaindoindoles (4-([8-amino-7-chloro-5-methyl-5H-as-triazino (5,6-b)indol-3-yl]amino)-2-methyl-2-butanol (SK&F 40491)), 2,6-diphenyl-3-methyl-2,3-dihydroimidazo[2,1-b]thiazole (RP 19236), 3-alpha-naphthyl-5-diethylcarbamoyl-1,2,4-oxadiazole (GL R9-338), Oxolinic acid, Isoquinolines (1-(p-chlorophenoxymethyl)-3,4-dihydroisoquinone hydrochloride (UK-2054), 3,4-dihydro-1-isoquinolineacetamide hydrochloride), 1-p-chlorophenyl-3-(m-3-isobutyl-guanidinophenyl)urea hydrochloride (ICI 73,602), and Zinc salts. Substances which prevent attachment of the rhinovirus to the nasal cells, such as anti ICAM-1 antibody [Hayden et al, Antiviral Res., 9:233-247 (1988)] and synthetic ICAM-1 [Greve et al., Cell, 56:839-847 (1989)], and other types of interferon should also be useful in COVAM therapy. In addition, agents which are known to be effective against influenza virus, another respiratory virus, such as amantadine, rimantadine, and ribavirin will be useful in COVAM therapy, as well as, antiviral agents which may become available to treat other cold viruses including coronavirus, parainfluenza virus, rhinovirus, adenovirus, influenza virus, and respiratory syncytial virus.

Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	KWIC	Image
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4. Document ID: US 5286748 A

Entry 4 of 6

File: USPT

Feb 15, 1994

DOCUMENT-IDENTIFIER: US 5286748 A

TITLE: General method of shortening the duration of common colds by application of medicaments to tissues of oral cavity

BSPR:

Enviroxime (2-amino-1-(isopropyl sulphenyl)-6-benzimidazole phenyl ketone oxime), a nontoxic but strong and broad spectrum antirhinoviral agent against 83 out of 83 rhinovirus serotypes, was particularly disappointing as it failed to demonstrate efficacy after topical nasal administration to common cold sufferers.

Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	KWIC	Image
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5. Document ID: US 5240694 A

Entry 5 of 6

File: USPT

Aug 31, 1993

DOCUMENT-IDENTIFIER: US 5240694 A

TITLE: Combined antiviral and antimediator treatment of common colds

DEPR:

While the antiviral agent used in the investigations was inteferon .alpha.2, other antiviral agents which are specific for viruses commonly found in colds should yield the same synergistic cold combatting results when used in combination with antiinflammatory compounds. As suitable examples of antiviral agents that could be used in COVAM therapy, Sperber et al., Antimicrob. Agents Chemother., 32:409-419 (1988), which is herein incorporated by reference, provides a listing of representative antiviral agents with activity against rhinovirus which includes the following: Inteferons (rIFN-.alpha..sub.2b, rIFN-.alpha..sub.2a, rIFN-.beta..sub.serine), Interferon inducers (Poly I:C, N,N-Dioctadecyl-N', N'-bis-(2-hydroxyethyl)-propanediamine (CP-20,961), Capsid binding agents/inhibitors of uncoating (4',6-Dichloroflavan (BW 683C), 4'-ethoxy-2'-hydroxy-4,6'-dimethoxychalcone (Ro 09-0410), 5-ethoxy-3-methoxy-2-(p-methoxy-trans-cinnamoyl)phenylphosphate (Ro 09-0415), 1-(5-tetradecyloxy-2-furanyl)ethanone (RMI 15,731), 2-[-(1,5,10,10a-tetrahydro-3H-thiazolo[3,4b]isoquinolin-3-ylindene)amino]-4-thiazole acetic acid (44,081 R.P.), Disoxaril, 5-[7-[4-(4,5 dihydro-2-oxazolyl)phenoxy]heptyl]-3-methylisoxazole (WIN 51,711), 3-methoxy-6-[4-(3-methylphenyl)-piperazinyl]pyridazine (R61837), 3,4-dihydro-2-phenyl-2H-pyrano[2,3-b]pyridines, and phenoxypyridinecarbonitriles), 2-(3,4-dichlorophenoxy)-5-nitrobenzonitrile (MDL 860), Benzoimidazoles (Enviroxime, 2-amino-1-(isopropyl sulfonyl)-6-benzimidazole phenyl ketone oxime), 1'-methyl spiro(adamantane-2,3-pyrrolidine)maleate, Isatin thiosemicarbazone, Fusidic acid, Substituted trizaindoles (4-([8-amino-7-chloro-5-methyl-5H-as-triazino(5,6-b)indol-3-yl]amino)-2-methyl-2-butanol (SK&F 40491)), 2,6-diphenyl-3-methyl-2,3-dihydroimidazo[2,1-b]thiazole (RP 19236), 3-alpha-naphthyl-5-diethylcarbamoyl-1,2,4-oxadiazole (GL R9-338), Oxolinic acid, Isoquinolines (1-(p-chlorophenoxymethyl)-3,4-dihydroisoquinone hydrochloride (UK-2054), 3,4-dihydro-1-isoquinolineacetamide hydrochloride), 1-p-chlorophenyl-3-(m-3-isobutyl-guanidinophenyl)urea hydrochloride (ICI 73,602), and Zinc salts. Substances which prevent attachment of the rhinovirus to the nasal cells, such as anti ICAM-1 antibody [Hayden et al, Antiviral Res., 9:233-247 (1988)] and synthetic ICAM-1 [Greve et al., Cell, 56:839-847 (1989)], and other types of interferon should also be useful in COVAM therapy. In addition, agents which are known to be effective against influenza virus, another respiratory virus, such as amantadine, rimantadine, and ribavirin will be useful in COVAM therapy, as well as, antiviral agents which may become available to treat other cold viruses including coronavirus, parainfluenza virus, rhinovirus, adenovirus, influenza virus, and respiratory syncytial virus.

Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	KWIC	Image
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6. Document ID: US 4333941 A

Entry 6 of 6

File: USPT

Jun 8, 1982

DOCUMENT-IDENTIFIER: US 4333941 A

TITLE: Inhibition of enveloped viruses with phenyl ketones

BSPR:

As employed herein, the phrase "pharmaceutically-acceptable salt" refers to salts of the phenylketones the anions of which are relatively non-toxic and innocuous to mammals at dosages or concentrations consistent with good antiviral activity so that side effects ascribable to the anions do not vitiate the beneficial effects of the phenylketones. Suitable pharmaceutically-acceptable salts which can be employed in the method and composition of the invention include those derived from mineral acids such as the hydrochloride, hydrobromide, phosphate, nitrate and sulfate salts, those derived from organic carboxylic acids such as the succinate, tartrate, citrate, malate, maleate, and acetate salts and those derived from organic sulfonic acids such as the methanesulfonate and toluenesulfonate salts.

BSPR:

In practicing the method, an enveloped virus is contacted with one or more of the phenylketones in an amount sufficient to inactivate the virus. Contacting can be carried out in vitro, in the absence of living tissue, for example, by contacting non-living substrates contaminated with virus. In vitro operations can be useful to inactivate viruses in contaminated liquids such as solutions or suspensions, for example, in saliva, urine or in virus culture media for protein coated viruses such as picorna viruses, to inhibit contaminating enveloped viruses. In vitro operations can also be used for solid substrates and surfaces such as bedding, garments; dental equipment, vaginal speculae, forceps, examination tables, gloves, milking machines, poultry cages and the like which may become contaminated with infective enveloped viruses, such as herpes simplex, influenza, infectious bovine rhinotracheitis, Newcastle's disease virus. Also the active compounds can be incorporated in air filters, screens or the like to inactivate air borne viruses passed therethrough.

BSPR:

The contacting of enveloped virus and phenylketone compound can also be carried out in vivo, by administering an effective amount of the phenylketone compound to a mammal infected with enveloped virus, in a manner effective to result in contact and exposure of the virus to a virus inhibiting amount of the compound. The compounds can be administered orally, parenterally (usually by injection) or topically. Dyclonine hydrochloride, for example, has been administered in anesthetic studies, intravenously at dosages of up to 7 milligrams compound per kilogram of body weight ("mg/kg") with no notable anesthetic effects, and orally at doses up to about 17 mg/kg also with no notable anesthetic effect. It has an acute LD₅₀ in mice of 19.5 mg/kg intravenous and 52.8 mg/kg by intraperitoneal injection. Topical application permits use of higher phenylketone concentrations directly at infected sites, such as genital herpes virus type 2 ("HSV-2") lesions, or intact genital mucosa infected or contaminated with HSV-2, without prior distribution of compound through uninfected parts of the mammalian system. Topical application of the phenylketones is preferred.

BSPR:

The amount of the phenylketone compound to be employed can be referred to as an "antiviral amount", "viral inhibiting amount", or "effective amount to inhibit viruses", etc., it being understood that sufficient compound is employed to achieve significant viral inhibition. The antiviral amount of compound, that is, the amount of the phenylketone compound sufficient to provide the desired effect depends on various known factors such as type of contacting, in vitro or in vivo operations, concentration of phenylketone, exposure time (contact time), type of virus involved, degree of viral contamination or infection, the size, type, age and condition of the animal to be treated, locus of infection in the animal, the particular compound of pharmacologically-acceptable salt employed, the route and frequency of administration, the degree of inhibition desired, and whether or not topical anesthetic action is also desirable. In particular cases, the amount to be administered can be ascertained by conventional range finding techniques, for example, by observing the effect produced at different treatment rates using

conventional virus assay procedures.

BSPR:

Preferred compositions include compositions containing from about 0.0025 to about 0.05 to about 0.25, to about 0.5 to about one to about 10 percent to about 25 percent by weight of phenylketone in a carrier. Generally, topical compositions containing from about 0.0025 to about 0.25 percent phenylketone in a topically acceptable pharmaceutical carrier have low anesthetic effect, and are preferred when topical anesthesia is to be avoided, and higher concentrations (0.5 to 5 percent) are used when concurrent anesthesia and antiviral action are desired. Concentrations of one to 25 to 95 percent are useful in concentrates to be diluted before use and in in vitro applications.

BSPR:

The method of the invention is useful in inhibiting or inactivating enveloped viruses, (also classifiable as ether sensitive virus or lipid containing viruses) such as rhabdo, herpes, influenza, .alpha. and paramyxo viruses. Picorna viruses with protein coats, (ether resistant viruses) such as rhino virus and polio virus appear to be relatively insensitive to contact with the phenylketones. Vaccinia virus is affected, but is much more resistant than enveloped viruses. Electron microscopy indicates that contact of enveloped virus with the phenylketones results in substantially complete rupture of the viral envelope and release of viral nucleoproteins. However, it is understood that the invention is not limited to a particular mechanism or theory of viral inactivation.

BSPR:

A particularly advantageous feature of the invention is the discovery that the phenylketones are effective against herpes simplex virus type 2 ("HSV-2"). HSV-2 is frequently involved in urogenital infections, the affected organs being the cervix, vulva, vagina, urethra in females and penis and urethra in males. It has also been involved in localized and generalized infections of newborns, the infection usually being transmitted during delivery on passage through the infected birth canal. HSV-2 infections have been recently recognized as a common venereal disease. See, Nahmias and Roizman, New England Journal of Medicine, 289(15): 781 (1973). HSV-1 is more commonly involved in oral, labial and ocular infections and is immunologically different from HSV-2. See, Nahmias and Roizman, supra, and Stalder et al., Journal of Infectious Diseases, 131(4): 423 (1975). Infectious virus can be transmitted by contact, through contaminated body fluids, air droplets or through medical or dental implements which have contacted the infected sites.

BSPR:

Inactivation of herpes viruses in vitro by means of the invention can be useful in controlling transmission of the virus. Inactivation of genital herpes virus, particularly HSV-2, by contacting genital herpes lesions or preferably by contacting intact but infected (or contaminated but uninfected) genital cutaneous mucosa with one or more of the phenylketones, can also be useful in controlling or inhibiting transmission of virus both between hosts and between different sites in the same host, or between mother and newborn and can also be useful in alleviating the infection. The local anesthetic effect of the phenylketones, particularly dyclonine hydrochloride can provide symptomatic relief from local irritation at the infected lesions. In some situations, the invention is advantageously employed by contacting infected skin or mucous membrane or contaminating viruses on uninfected skin or mucous membrane, with an antiviral amount less than an anesthetic amount of the phenylketone, to bring about viral inhibition without anesthesia. In the latter situations the compounds are preferably employed in solutions, or suspensions or lotions such as soap or detergent cleansers, rinses, lotions, douches, skin creams, alcoholic solutions, aqueous solutions, etc. at concentrations from about 0.001 percent by weight to about 0.1 to 0.3 percent by weight.

CLPR:

1. A method for inhibiting enveloped viruses on non-living substrates which comprises contacting an enveloped virus and a non-living substrate contaminated therewith, with an effective virus inhibiting amount of a phenylketone compound or pharmacologically-acceptable salt thereof, said phenylketone compound corresponding to one of the formulae: ##STR4## wherein R represents hydrogen, halo, or alkoxy of from one to twelve carbon atoms, R' represents hydrogen or halo; R.sub.1 and R.sub.2 represent loweralkyl, or R.sub.1 and R.sub.2 taken

together with the nitrogen atom represent a heterocyclic amino group or an N-alkyl quaternary heterocyclic ammonium group having four, five or six carbon atoms and zero or one additional ring hetero atom selected from oxygen, sulfur and nitrogen or R.sub.1 and R.sub.2, taken together with the nitrogen atom represent triloweralkylammonium.

CLPR:

9. A method for inhibiting enveloped viruses which comprises contacting enveloped viruses with an effective virus inhibiting amount of a phenylketone compound or pharmacologically-acceptable salt thereof, said phenylketone compound corresponding to one of the formulae: ##STR5## wherein R represents hydrogen, halo, or alkoxy of from one to twelve carbon atoms, R' represents hydrogen or halo; R.sub.1 and R.sub.2 represent loweralkyl, or R.sub.1 and R.sub.2 taken together with the nitrogen atom represent a heterocyclic amino group or N-alkyl quaternary heterocyclic ammonium group having four, five or six carbon atoms and zero or one additional ring hetero atom selected from oxygen, sulfur and nitrogen, or R.sub.1 and R.sub.2 taken together with the nitrogen represent triloweralkylammonium, with the proviso that, when the phenylketone compound corresponds to formula I, wherein R' is hydrogen and R.sub.1 and R.sub.2, taken together with the nitrogen atom represent piperidino, R.sub.2 is other than n-butoxy.

Full	Title	Citation	Front	Review	Classification	Date	Reference	Claims	KWIC	Image
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